AUTOIMMUNE CONNECTIVE TISSUE DISEASES

MIR-142-3P IS CRITICAL FOR THE PRO-INFLAMMATORY PHENOTYPE OF MONOCYTE-DERIVED DENDRITIC CELLS IN SYSTEMIC LUPUS ERYTHEMATOSUS THROUGH TARGETING THE GENE OF GP130

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Background: We previously found microRNA-142-3p was elevated and regulated the pro-inflammatory function of monocyte-derived dendritic cells (moDCs) in patients with SLE.

Objective: To know the molecular mechanisms that miR-142-3p functioned in moDCs of SLE.

Materials and Methods: Lentiviral constructs were used to alter the expression level of miR-142-3p in moDCs. Luciferase reporter assay, qPCR and western blot were used to confirm the target gene of miR-12-3p. ELISA was used to examine the level of soluble glycoprotein 130 (gp130). PCR array was used to examine the inflammatory cytokines and chemokines.

Results: The luciferase reporter experiment suggested that the target gene of miR-142-3p was gp130 and the binding site was 3'UTR. The levels of gp130 mRNA significantly increased 2.93-fold (P=0.01) in moDCs with miR-142-3p down-regulated, while it reduced 0.14-fold (P=0.003) in miR-142-3p overexpression group. At the protein level, overexpression of miR-142-3p repressed the level of gp130 (P=0.021), while down-regulation of miR-142-3p induced the expression of gp130 (P=0.011). The level of sgp130, a natural inhibitor of IL-6 trans-signaling, was 169.54±85.62 ng/ml in negative controls, while it was significantly lower (76.93±27.92 ng/ml, P=0.008) in the plasma of patients with SLE. Similarly, in the supernatants of moDCs with miR-142-3p over-expressed, the level of sgp130 (604.67±194.65 pg/ml, P=0.02) decreased significantly compared with mock (1245.67±280.60 pg/ml) and moDCs with down-regulated miR-142-3p (1195.67±195.98 pg/ml). We also found the gene of IL6, TNF, IL8, CXCR4, MAPK1, CCL2, JAK2, MTOR, IL1B, CCL3, CCL4, CCL5, IL6R in moDCs were significantly increased while the gene of MYC, IL4, BCL2, IL17A, IL22, IL18, IL2, CXCL10, IL5, CXCL12 were significantly decreased in miR-142-3p overexpressed group.

Conclusions: The results demonstrated that miR-142-3p could target the gene of gp130 and control the inflammatory cytokine signaling cascades in moDCs. These findings suggested that miR-142-3p could serve as a novel therapeutic target for the treatment of SLE.